



RYR1 gene

ryanodine receptor 1

Normal Function

The *RYR1* gene provides instructions for making a protein called ryanodine receptor 1. This protein is part of a family of ryanodine receptors, which form channels that transport positively charged calcium atoms (ions) within cells. Channels made with the ryanodine receptor 1 protein play a critical role in muscles used for movement (skeletal muscles).

For the body to move normally, skeletal muscles must tense (contract) and relax in a coordinated way. Muscle contractions are triggered by the flow of positively charged ions, including calcium, into muscle cells.

When muscles are at rest, calcium ions are stored in a cellular structure called the sarcoplasmic reticulum inside each muscle cell. In response to certain signals, the RYR1 channel releases calcium ions from the sarcoplasmic reticulum into the surrounding cell fluid (cytoplasm). The resulting increase in calcium ion concentration stimulates muscle fibers to contract, allowing the body to move. The process by which certain chemical signals trigger muscle contraction is called excitation-contraction (E-C) coupling.

Health Conditions Related to Genetic Changes

central core disease

More than 90 mutations in the *RYR1* gene have been identified in people with central core disease (CCD). Most of these mutations affect single protein building blocks (amino acids) in critical regions of the ryanodine receptor 1 protein. These mutations change the structure of the RYR1 channel, which alters the normal flow of stored calcium ions within muscle cells. A disruption in calcium ion release prevents muscles from contracting normally, leading to the muscle weakness characteristic of central core disease.

Researchers have proposed two mechanisms to explain how *RYR1* gene mutations underlie muscle weakness in people with central core disease. Some genetic changes cause the RYR1 channel to be "leaky," allowing calcium ions to flow slowly but continually out of the sarcoplasmic reticulum. The leaky channels greatly reduce the amount of stored calcium ions. As a result, not enough calcium ions are available in the sarcoplasmic reticulum to trigger muscle contractions. Muscle weakness results from the inability of skeletal muscles to contract appropriately.

Other *RYR1* gene mutations change the structure of the RYR1 channel in a way that impedes the normal flow of calcium ions. Although the sarcoplasmic reticulum stores plenty of these ions, the receptor cannot release them in response to the usual signals. Without enough calcium ions flowing out of the sarcoplasmic reticulum at the appropriate time, muscles cannot contract normally and muscle weakness results. This mechanism is known as E-C uncoupling.

centronuclear myopathy

congenital fiber-type disproportion

At least seven mutations in the *RYR1* gene have been found to cause congenital fiber-type disproportion, a disorder that causes general muscle weakness that typically does not worsen over time. Some mutations change single amino acids in the ryanodine receptor 1 protein. Other *RYR1* gene mutations create a premature stop signal in the instructions for making the receptor, resulting in an abnormally short, nonfunctional protein. Researchers suspect that disruption of the RYR1 channel may play a role in the muscle weakness and other features of congenital fiber-type disproportion, although the role of *RYR1* gene mutations in this condition is unclear.

malignant hyperthermia

At least 217 mutations in the *RYR1* gene are known to increase the risk of malignant hyperthermia. Most of these mutations change single amino acids in important regions of the ryanodine receptor 1 protein. These mutations alter the structure of the RYR1 channel, causing it to open more easily and close more slowly in response to certain drugs (particularly some anesthetic gases and a type of muscle relaxant used during surgery). As a result, large amounts of calcium ions are released from the sarcoplasmic reticulum within muscle cells. An overabundance of available calcium ions causes skeletal muscles to contract abnormally, which leads to muscle rigidity in people with malignant hyperthermia. An increase in calcium ion concentration within muscle cells also activates processes that generate heat (leading to increased body temperature) and produce excess acid (leading to acidosis).

Many other changes in the *RYR1* gene have been described in people with an increased risk of malignant hyperthermia. It is unclear, however, whether these variations are directly related to malignant hyperthermia risk.

multiminicore disease

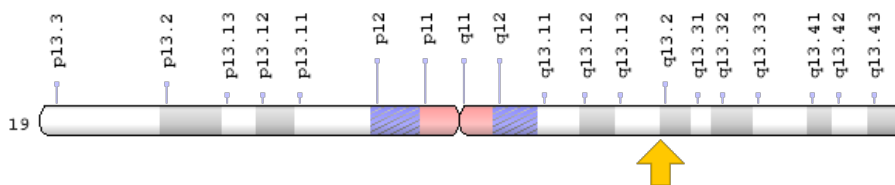
Several mutations in the *RYR1* gene have been found to cause atypical forms of multiminicore disease. These mutations change single amino acids in the ryanodine receptor 1 protein, which alters the structure and function of the protein. The effects of these changes are unclear. Some mutations may reduce the amount of ryanodine receptor 1 protein produced by the cell or lead to an unstable version of the protein.

Other mutations may interfere with the normal regulation of the RYR1 channel. Researchers believe that some *RYR1* gene mutations change the shape of the channel in such a way that calcium ions cannot flow through properly. A disruption in calcium ion transport prevents muscles from contracting normally, leading to the muscle weakness characteristic of multiminicore disease.

Chromosomal Location

Cytogenetic Location: 19q13.2, which is the long (q) arm of chromosome 19 at position 13.2

Molecular Location: base pairs 38,433,700 to 38,587,564 on chromosome 19 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- CCD
- MHS
- MHS1
- PPP1R137
- ryanodine receptor 1 (skeletal)
- ryanodine receptor type1
- RYDR
- RYR
- RYR-1
- RYR1_HUMAN
- sarcoplasmic reticulum calcium release channel
- skeletal muscle ryanodine receptor
- Skeletal muscle-type ryanodine receptor
- SKRR

Additional Information & Resources

Educational Resources

- Eureka Bioscience Collection: Intracellular Ca²⁺ Release Channels
<https://www.ncbi.nlm.nih.gov/books/NBK5959/>
- Neuromuscular Disease Center, Washington University: Central Core Disease
<http://neuromuscular.wustl.edu/syncm.html#cc>
- Neuromuscular Disease Center, Washington University: Congenital Fiber Type Size Disproportion
<http://neuromuscular.wustl.edu/syncm.html#cftd>
- Neuromuscular Disease Center, Washington University: Malignant Hyperthermia
<http://neuromuscular.wustl.edu/msys/myoglob.html#mh>
- Neuromuscular Disease Center, Washington University: Multicore (Minicore) Disease
<http://neuromuscular.wustl.edu/syncm.html#multicore>

GeneReviews

- Central Core Disease
<https://www.ncbi.nlm.nih.gov/books/NBK1391>
- Congenital Fiber-Type Disproportion
<https://www.ncbi.nlm.nih.gov/books/NBK1259>
- Malignant Hyperthermia Susceptibility
<https://www.ncbi.nlm.nih.gov/books/NBK1146>
- Multiminicore Disease
<https://www.ncbi.nlm.nih.gov/books/NBK1290>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28RYR1%5BTIAB%5D%29+OR+%28ryanodine+receptor+1%5BTIAB%5D%29%29+AND+%28ryr1%5BMAJR%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D>

OMIM

- RYANODINE RECEPTOR 1
<http://omim.org/entry/180901>

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
http://atlasgeneticsoncology.org/Genes/GC_RYR1.html
- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=RYR1%5Bgene%5D>
- HGNC Gene Family: Protein phosphatase 1 regulatory subunits
<http://www.genenames.org/cgi-bin/genefamilies/set/694>
- HGNC Gene Family: Ryanodine receptors
<http://www.genenames.org/cgi-bin/genefamilies/set/287>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=10483
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/6261>
- UniProt
<http://www.uniprot.org/uniprot/P21817>

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